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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
ROBINSON, HOPE A	
ART UNIT	**PAPER NUMBER**
1652	

MAIL DATE	DELIVERY MODE
06/19/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/788,793	SATO ET AL.	
	Examiner	Art Unit	
	Hope A. Robinson	1652	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on 61406.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) 28-31 is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) 28-31 is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Application Status

1. The Art Unit location of your application in the USPTO has changed. To aid in correlating any papers for this application, all further correspondence regarding this application should be directed to Art Unit 1652.

2. Applicant's response to the Office Action mailed May 16, 2006on June 16, 2006, is acknowledged.

Claim Disposition

3. Claims 28-31 are pending and are under examination.

New-Abstract Objection

4. The Abstract is objected to because of the following informalities:

The newly submitted abstract has the following typographical error on line 1, "The present invention relates to which have a role in controlling". Note that the sentence is incomplete.

Correction is required.

Maintained-Specification Objection

5. The Specification remains objected to because of the following informalities:

The specification remains objected to because "paragraphs" are referred to throughout the specification, see for example page 7 of the newly submitted specification where the following appears "(paragraph 1)"; "(paragraph 2)" through "(paragraph 7)". This numbering is confusing as for example, "paragraph 1" provides priority document information (see page 1), yet page 7 discloses "...(b) a protein which comprises an amino-acid sequence wherein 1 or several amino acids are deleted, substituted or added in an amino-acid sequence shown in SEQ ID NO:2 in the sequence listing, and has effects of controlling cell migration and cell death (paragraph 1)". What is the examiner to glean from the reference to "paragraph 1"?

Correction is required.

Response to Applicant's Arguments

6. On page 2 of the response filed on February 14, 2006 applicant state that references to "paragraphs" remain in the specification because they are a "numbered paragraph which form part of the description of the invention". It is suggested that this notation is removed from the specification because the numbering of paragraphs in the specification should follow this notation "[001]" for example, furthermore, there is no indication that the referred to "paragraph 2" for example is item number 2 on page 42 instead of the paragraph that appears on page 1 of the specification for example. In addition, throughout the text of the specification reference is made to "paragraphs" which is confusing. See for example page 8 where the following appears, "...the protein according to paragraph 11, 13 or 15, wherein control of cell migration and cell death is caused by the degradation of Filamin 1 (paragraph 16)" or "[T]he present invention further relates to: a peptide that comprises a part of the protein according to any one of

paragraphs 10 to 16, and has effects of controlling cell migration and cell death (paragraph 17)...". Thus the objection remains.

Correction of the above is required.

Maintained and Amended-Claim Objections

7. Claim 28-29 remains objected to because of the following informalities:

Claim 28 is objected to for the recitation of "and/or" because the Markush language is improper and "selected from the group consisting of should be "A, B and C".

Claim 29 is objected to as the phrase "amino acid" appears with a hyphen (amino-acid). See item "b" of the claim.

Correction is required.

Maintained-Claim Rejections - 35 USC э 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

8. Claims 28-29 and 31 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The claimed invention is directed to an isolated DNA molecule contained in (SEQ ID NOS:1, 3 and 5), a variant sequence consisting essentially of either of the sequences recited, wherein the variant sequence hybridizes with the sequences recited under stringent conditions or hybridizes with a probe. . The claims are also directed to said variant that encodes a protein that binds to Filamin 1 and inhibits cell migration. Claims 28-29 and 31 do not set forth the specific hybridization conditions considered to be stringent. The art recognizes that hybridization conditions can vary. It is noted that the instant specification provides a discussion on hybridization conditions, however, it is merely exemplary, not limiting, thus does not breathe life into the claims. In addition, a sequence that hybridizes to the sequence of interest may not necessarily encode the same protein. In addition, the claims encompass a genus of variant DNA sequences (see item b) said to consist essentially of the DNA molecule. The skilled artisan cannot envision the detailed chemical structure of the claimed variants, thus the claimed invention lacks adequate written description. The specification fails to provide any additional representative species of the claimed genus to show that applicant was in possession of the claimed genus. A representative number of species means that the species, which are adequately described, are representative of the entire genus. The written description requirement for a claimed genus may be satisfied through sufficient description of a representative number of species by actual reduction to practice, disclosure of drawings, or by disclosure of relevant

identifying characteristics, for example, structure or other physical and/or chemical properties, by functional characteristics coupled with a known or disclosed correlation between function and structure, or by a combination of such identifying characteristics, sufficient to show the applicant was in possession of the claimed genus. Furthermore, the claims encompass a sequence that has all of the complement, thus identical to the complement of the encoding DNA and said complement cannot encode the same protein. Further, *Vas-Cath Inc. v. Mahurkar, 935 F.2d 1555, 1563-64, 19 USPQ2d 1111, 1117 (Fed. Cir.1991)*, states that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in *possession of the invention*. The invention is, for purposes of the 'written description' inquiry, *whatever is now claimed*" (See page 1117). The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed" (See *Vas-Cath* at page 1116). The skilled artisan cannot envision the detailed chemical structure of the encompassed genus of nucleic acids, and therefore, conception is not achieved until reduction to practice has occurred, regardless of the complexity or simplicity of the method of isolation. Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method of isolating it. The compound itself is required. *See Fiers v. Revel, 25 USPQ2d 1601 at 1606 (CAFC 1993).*

Therefore, for all these reasons the specification lacks adequate written description, and one of skill in the art cannot reasonably conclude that the applicant had possession of the claimed invention at the time the instant application was filed.

9. Claims 28-31 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for the DNA encoding proteins set forth in SEQ ID NOS: 2, 4 and 6 that controls cell migration and cell death, does not reasonably provide enablement for any variant thereof of the claimed DNA. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make the invention commensurate in scope with these claims. The enablement requirement refers to the requirement that the specification describe how to make and how to use the invention. There are many factors to be considered when determining whether there is sufficient evidence to support a determination that a disclosure does not satisfy the enablement requirement and whether any necessary experimentation is undue. These factors include, but are not limited to: Quantity of Experimentation Necessary; Amount of direction or guidance presented; Presence or absence of working examples; Nature of the Invention; State of the prior art and Relative skill of those in the art; Predictability or unpredictability of the art and Breadth of the claims (see *In re Wands, 858 F.2d at 737, 8 USPQ2d at1404 (Fed. Cir. 1988)*. The factors most relevant to the instant invention are discussed below.

The amount of experimentation required to practice the claimed invention is undue as the claims encompass an unspecified amount of variants of the claimed product, which may not retain the ascribed function (encoding a protein that binds filamin 1). Additionally, on page 6 of the instant specification it is disclosed that the DNA of the present invention encodes a protein that has a sequence, which can be deleted, substituted or added with regard to one or more amino acids. Thus, the claimed invention encompasses a large amount of variability for the DNA and

the encoding protein sequence and there is no correlation made between the structure and function of the claimed products following modification. Moreover, based on the large variability contemplated said DNA may encode a protein that is different and that won't bind Filamin 1. The specification does not describe properties of the claimed variants, such as size; or demonstrate any such variant retaining the activity. Claim 28(b) recites the language "consisting essentially of either of the sequences" and under stringent conditions which are not recited in the claim. The art recognizes Filamin A regulates cortical cell migration out of the ventricular zone (Nagano et al., Nat. Cell Biol., 2002, July, vol. 4, no.7, pages 495-501). A search of the claimed sequences discloses proteins that are 69.9% or 19% identical to the claimed sequence, however, have a different function and these proteins are encompassed in the claim. For example, HYSEQ INC. disclose a protein that has 73.68% identity to SEQ ID NO:1 and SEQ ID NO:2 (DNA and the encoding the protein, respectively), however, the reference indicates that the protein is useful for treating diseases of the peripheral nervous system, such a neuropathies like Alzheimer's, Parkinson's disease, Huntington's disease, Shy-Drager Syndrome, Amyotrophic lateral sclerosis etc., therefore, the instant claims and specification needs to provide sufficient information regarding the activity to the protein to be altered in the claims. Thus, due to the large quantity of experimentation necessary to generate the infinite number of variants recited in the claims and possibly screen same for activity and the lack of guidance/direction provided in the instant specification, this is merely an invitation to the skilled artisan to use the current invention as a starting point for further experimentation. Thus, undue experimentation would be required for a skilled artisan to make and/or use the claimed invention commensurate in scope with the claims.

Predictability of which potential changes can be tolerated in a protein's amino acid sequence and obtain the desired activity requires a knowledge of and guidance with regard to which amino acids in the protein's sequence, if any, are tolerant of modification and which are conserved (for example, expectedly intolerant to modification), and detailed knowledge of the ways in which the protein's structure relates to its function. In addition, one skilled in the art would expect any tolerance to modification for a given protein to diminish with each further and additional modification, for example, multiple substitutions. In this case, the necessary guidance has not been provided in the specification. Therefore, while it is known in the art that many amino acid substitutions are possible in any given protein, the positions within the protein's sequence where such amino acid substitutions can be made with a reasonable expectation of success are limited, as certain positions in the sequence are critical to the protein's structure/function relationship. It is also known in the art that a single nucleotide or amino acid change or mutation can destroy the function of the biomolecule in many cases. For example, various sites or regions directly involved in binding activity and in providing the correct three-dimensional spatial orientation of binding and active sites can be affected (see Wells, Biochemistry, vol. 29, pages 8509-8517, 1990). The instant specification provides no guidance/direction as to which regions of the protein would be tolerant of modifications and which would not, and it provides no working examples of any variant sequence that is encompassed by the claims. It is in no way predictable that randomly selected mutations, such as deletions, substitutions, additions, etc., in the disclosed sequences would result in a protein having activity comparable to the one disclosed. As plural substitutions for example are introduced, their interactions with each other and their effects on the structure and function of the

protein is unpredictable. The skilled artisan would recognize the high degree of unpredictability that all the variants encompassed in the claims would retain the recited function.

The state of the prior art provides evidence for the high degree of unpredictability as stated above. Seffernick et al. (J. Bacteriology, vol. 183, pages 2405-2410, 2001) disclose two polypeptides having 98% sequence identity and 99% sequence identity, differing at only 9 out of 475 amino acids (page 2407, right column, middle and page 2408, Fig. 3). The polypeptides of Seffernick et al. are identical along relatively long stretches of their respective sequences (page 2408, Fig. 3), however, these polypeptides exhibit distinct functions. The modifications exemplified in the Seffernick et al. reference is small compared to those contemplated and encompassed by the claimed invention. Further, Saus et al. (US PGPUB No. 2003010855A1, 2002) disclose a DNA encoding a protein that is 31.72% identical to SEQ ID NO:1, which encodes SEQ ID NO:2 of the instant application, and it is disclosed that the protein is a GIP family protein, proteins with transcription factor activity. The DNA encoding the protein of the Saus et al. reference is encompassed in the claimed limitation of 1 or several deletions, which demonstrates the unpredictability of the fragment.

The specification lacks adequate guidance/direction to enable a skilled artisan to practice the claimed invention commensurate in scope with the claims. Furthermore, while recombinant and mutagenesis techniques are known in the art, it is not routine in the art to screen large numbers of mutated proteins where the expectation of obtaining similar activity is unpredictable based on the instant disclosure. The amino acid sequence of a protein determines its structural and functional properties, and predictability of what mutations can be tolerated in a protein's sequence and result in certain activity, which is very complex, and well outside the realm of

routine experimentation, because accurate predictions of a protein's function from mere sequence data are limited, therefore, the general knowledge and skill in the art is not sufficient, thus the specification needs to provide an enabling disclosure.

The working examples provided do not rectify the missing information in the instant specification pertaining to the claimed variant. The nature and properties of the claims is difficult to ascertain from the examples provided as one of skill in the art would have to engage in undue experimentation to construct the variants/fragments of the claimed invention and examine the same for function.

The specification does not provide support for the broad scope of the claims, which encompass an unspecified amount of fragments. The claims broadly read on any variant thereof for the claimed DNA. The issue in this case is the breath of the claims in light of the predictability of the art as determined by the number of working examples, the skill level artisan and the guidance presented in the instant specification and the prior art of record. This make and test position is inconsistent with the decisions of *In re Fisher, 427 F.2d 833, 839, 166 USPQ 18, 24 (CCPA 1970)* where it is stated that "...scope of claims must bear a reasonable correlation to scope of enablement provided by the specification to persons of ordinary skill in the art...". Without sufficient guidance, determination of having the desired biological characteristics is unpredictable and the experimentation left to those skilled in the art is unnecessarily and improperly extensive and undue. See *In re Wands, 858 F.2d at 737, 8 USPQ2d at 1404 (Fed. Cir. 1988).*

Thus, for all these reasons, the specification is not considered to be enabling for one skilled in the art to make and use the claimed invention as the amount of experimentation

required is undue, due to the broad scope of the claims, the lack of guidance and working examples provided in the specification and the high degree of unpredictability as evidenced by the state of the prior art, attempting to construct and test variants of the claimed invention would constitute undue experimentation. Making and testing the infinite number of possible fragments to find one that functions as described is undue experimentation. Therefore, applicants have not provided sufficient guidance to enable one of skill in the art to make and use the claimed invention in a manner that reasonably correlates with the scope of the claims, to be considered enabling.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter, which the applicant regards as his invention.

10. Claims 28-31 are rejected under 35 U.S.C. 112, second paragraph, as failing to set forth the subject matter, which applicant (s) regard as their invention.

Claim 28 is indefinite for the recitation of: "stringent hybridization conditions" as the claim does not set forth what conditions are deemed to be stringent, thus the metes and bounds of the claim is undefined, as the art recognizes that the conditions can vary such as the wash conditions. Further, the discussion provided in the instant specification is not limiting, therefore does not breathe life into the claims or establish a standard for the claimed invention. The dependent claim hereto is also included in this rejection as it does not rectify the deficiency.

Maintained-Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

11. Claims 28, 29 and 31 are rejected under 35 U.S.C. 102(b) as being anticipated by Dyson et al. (The Journal of Cell Biology, vol. 155, no. 6, pages 1065-1079, 2001), based on the broad recitation of a variant sequences in item (b) of claim 28.

The broadest reasonable interpretation of claims 28 and 29, is a sequence that binds filamin as item (c) of claim 28 and item (b) of claim 29 requires very little structure with the functional limitation. Dyson et al. disclose a DNA encoding a protein, which binds filamin, thus reads on the claims. As the claimed language of "all or part of" can be interpreted as 5 nucleotides the structure disclosed in the reference would hybridize to the claimed sequences set forth in SEQ ID NOS: 1, 3 or 5. In addition, the reference teaches expression in a host cell (claim 31). Therefore, the limitations of the claims are met by this reference.

Response to Applicant's Arguments

12. The response filed has been considered. Note that the rejections of record remain and have been amended to reflect changes made to the claims. The response essentially argues that the claims have structure and function, thus have written description. Tis argument is not persuasive because item (b) of claim 28 for example encompasses a genus of variants not adequately described. In addition, the claim does not set for the conditions that are considered to

be stringent. Therefore, the rejection remains. With regard to the enablement rejection, applicant's comments are noted but are not persuasive because the genus claimed is not adequately described, hence not adequately supported by the instant specification. The claims are not limited to a specific size for the variants, which may not exhibit the desired properties, however, such variability is encompassed in the claims.

Note also that rejections remain under 35 U.S.C. 112, second paragraph for the reasons of record and herein. The rejections remain because applicant did not amend all the claims to obviate this ground of rejection . This response is deemed sufficient to address the issues raised by applicant.

Conclusion

13. No claims are allowable.

14. Applicant's amendment necessitated the new/modified ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37

CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Hope A. Robinson whose telephone number is 571-272-0957. The examiner can normally be reached on Monday-Friday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ponnathapu Achutamurthy, can be reached at (571) 272-0928. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Hope Robinson, MS

Primary Examiner 6/11/07

HOPE ROBINSON
PRIMARY EXAMINER